No. 08/578,709, filed December 28, 1995 (now U.S. Patent 5,814,509). the disclosure of each of these applications is incorporated herein by reference.

Page 4, fourth paragraph delete and insert the following:

Accordingly, the present invention relates to a DNA comprising a DNA having a nucleotide sequence encoding an amino acid sequence of human-originated PGIS substantially depicted in Sequence No. ~~12~~15, preferably a DNA comprising a DNA having a 28th-1527th nucleotide sequence substantially shown in Sequence No. ~~11~~14, and more preferably a DNA having a 28th-1527th nucleotide sequence shown in Sequence No. ~~11~~14.

Page 4, sixth paragraph delete and insert the following:

The present invention also relates to a polypeptide having an amino acid sequence of human -oriented PGIS which is substantially shown in Sequence No. ~~12~~15, and antibodies having reactivities with said human-originated PGIS.

On page 6, second paragraph delete and insert the following:

The polypeptide of the present invention has a catalytic activity to convert PGH_2 to PGI_2 and has an amino acid sequence of human-originated PGIS substantially shown in Sequence Listing, Sequence No. ~~12~~ 15 to be mentioned later.

On page 6, third paragraph delete and insert the following:

By "substantially" is meant that the polypeptide of the present invention is not limited to the polypeptide having the amino acid sequence shown in Sequence No. ~~12~~15, but may include

deletion, substitution and addition with respect to some of the amino acids in the amino acid sequence shown in Sequence No. ~~12~~15, as long as the polypeptide has immunological and biological activity (human PGIS activity) similar to that of human-originated PGIS having said amino acid sequence.

On page 6, fourth paragraph delete and insert the following:

While the site of deletion, substitution and addition of the amino acids is not particularly limited, at least 441st Cys residue and thereabout region in the amino acid sequence shown in Sequence No. ~~12~~15need to be reserved. This is because human-originated PGIS of the present invention is homologous to known cytochrome P450 in the amino acid sequence, since it has Cys residue in the C-terminal side of the amino acid sequence constituting the heme-binding site (fifth ligand) which is important for the expression of biological activity of cytochrome P450, and speculated to be a new protein belonging to the cytochrome P450 family [see *Seibutsu Butsuri*, vol. 32, No. 1, pp. 10-15 (1992)].

On page 6, fifth paragraph delete and insert the following:

The polypeptide of the present invention preferably has an amino acid sequence of human-originated PGIS shown in Sequence No. ~~12~~15.

On page 7, first paragraph delete and insert the following:

The present invention also relates to a DNA comprising a DNA having a nucleotide sequence encoding the amino acid sequence of human-originated PGIS substantially shown in Sequence No. ~~12~~15.

On page 7, second paragraph delete and insert the following:

Said DNA may be any as long as it comprises a DNA having a nucleotide sequence encoding the aforementioned amino acid sequence of human-originated PGIS, and is exemplified by a DNA encoding the polypeptide having the amino acid sequence shown in Sequence No. ~~12~~15 or a polypeptide having the equivalent immunological and biological activity. More specifically, it is a DNA comprising the 28th-1578nd nucleotide sequence in the nucleotide sequence shown in Sequence No. ~~11~~14.

On page 7, third paragraph delete and insert the following:

In general terms, the genetic recombinant technique enables conversion of at least one nucleotide of a DNA sequence of a gene to a different nucleotide according to the degeneracy of the genetic code, without changing the amino acid sequence of a protein produced by the gene. Accordingly, the DNA of the present invention encompasses a DNA comprising a nucleotide sequence obtained by modification for substitution, based on the genetic code, of the 28th-1527th nucleotide sequence of Sequence Listing Sequence No. ~~11~~14.

On page 10, first paragraph delete and insert the following:

Human aorta vascular cells are lysed preferably using SDS or protenase K, and DNA is deproteinized by repetitive extraction with phenol. RNA is preferably digested with ribonuclease. The obtained DNA is partially digested with a suitable restriction enzyme and the obtained DNA fragment is amplified by a suitable phage or cosmid to form a library. Then, the clone having the desired sequence is detected by, for example, a method using a DNA probe with

a radioactive label, and a whole or partial PGIS gene is cleaved from said clone by using a restriction enzyme and the like (3). The DNA of the present invention can be prepared by chemical synthesis by a conventional method based on the nucleotide sequence depicted in Sequence Listing No.~~11~~14.

On pages 23 line 28-33 to Page 24, lines 1-9 delete and insert the following:

The obtained DNA insert was subcloned into pBluescriptII SK(-). By these steps, a clone (pHPGIS135) containing 3'-downstream region DNA of human-originated PGIS and a clone (pHPGIS36) containing 5'-upstream region DNA of human-originated PGIS were obtained. Then, the nucleotide sequence of the DNA insert of respective clones was determined by the Sanger method [Sanger, F., Nickle,, S., and Cloulson, A.R. (1977) Proc. Natl. Acad. Sci. USA 74, 5463-5467] using Taq dye primer cycle sequence kit (manufactured by Applied Biosystems) and Model 373A DNA sequencer (manufactured by Applied Biosystems). As a result, it was found that pHPGIS36 clone had, as a DNA insert sequence, a 740 bp nucleotide sequence (SQ No.~~9~~10) of cDNA of human PGIS, having an adapter sequence on the 5' side, based on which partial amino acid sequence of PGIS comprising ~~238~~237 amino acid residues wherein ATG is the translation initiation sequence (Met) was identified.

On page 24, first paragraph please delete and insert the following:

It was also found that pHPGIS135 clone comprised, as a DNA insert sequence, a 1277 bp nucleotide sequence (SQ No. 10) of cDNA of human PGIS, having an adapter sequence on the 3' side, based on which partial amino acid sequence of PGIS on the carboxyl side region starting

from 226th aspartic acid was identified. The nucleotide sequence of human PGIS cDNA contained in pHPGIS36 clone and the amino acid sequence deduced therefrom are depicted in SQ No. ~~10~~13 therein. Fig. 1 shows a restriction enzyme map of human PGIS cDNA and the region of human PGIS cDNA, which corresponds to the DNA contained in pHPGIS141, pHPGIS36 and pHPGIS135 Fig. 2 shows restriction enzyme map of pHPGIS136 and Fig. 3 shows restriction enzyme map of pHPGIS135.

On page 24, second paragraph delete and insert the following:

Human PGIS cDNA obtained by the above-mentioned cloning had a consensus sequence of the initiation codon of eukaryotic shown by Kozak et al. [Nucleic Acids Res. 12, 857-872 (1984) at around the translation initiation codon, and TGA codon corresponding to the termination codon at 500 codons therefrom. Based on these facts, it was found that the cDNA of the cloned human PGIS comprised 1977 bp comprising 1500 bp encoding 500 amino acid residues, as shown in SQ No. ~~12~~15, and the molecular weight of the protein coded thereby was speculated to be about 57,000.

On page 27 lines 29-33 to page 28 lines 1-12 delete and insert the following:

The obtained pHPGIS36 clone was cleaved out with restriction enzymes SalI and NspI and purified to give a SaLI-NspI fragment. The pHPGIS 135 clone was cleaved out with restriction enzymes PstI and BamHI and purified to give a PstI-BamHI fragment. Furthermore, primers [SQ No. ~~13~~16: P5 primer (676-600), SQ No.~~14~~17: P6 primer (832-855)] having sequences depicted in Sequence Listing Sequence Nos. ~~13~~16 and ~~14~~17 were synthesized based